A Girl with Green Complexion and Iron Deficiency: Chlorosis Revisited

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Case Report

A previously healthy, 9-year-old girl of Mediterranean/Filipino descent was referred for a 2-month history of her face, hands, and fingers "becoming green." A digital photograph clearly shows the child's bizarre green facial completion (Figure 1). She ate a varied diet and denied, on repeated and detailed questioning, pica, binge eating, purging, vomiting, or self-starvation. There was no history of excessive weight loss or weight gain. Our patient and her mother also denied excessive consumption of green-colored foods or vegetables or items with green food coloring, jaundice, discolored urine, melena, hematoschezia, menarche, pallor, or fever. Although she continued to participate in physical activities such as softball, she had recently complained of mild fatigue, and her mother described a slight decrease in appetite. The patient had a history of occasional nosebleeds. There was no other recognized blood loss. Within the 2-month history, our patient had had several episodes of recurrent mouth sores without gingival bleeding. The mother had thalessemia trait and there was a family history of von Willebrand's disease, although our patient had had a tonsillectomy at age 5 years without any bleeding complications.

Physical findings were as follows: weight 38.2 kg (>90th percentile), height 133.9 cm (60th percentile) heart rate 92 beats per minute, respiratory rate 24/minute, blood pressure 124/73 mmHg, and pulse oximetry O_2 saturation 99%. She had no fever and her urine had the usual color. The child had a remarkable and unmistakable green complexion of the forehead, nasal bridge, and the medial aspects of both cheeks and chin. The green color was evident on the dorsum of both hands and all fingers. The color of the remainder of her body was normal. There was no conjunctival icterus, the oral and nasal mucous membranes were unremarkable without ulcerations or evidence of recent bleeding, and no jaundice was apparent. Findings from the remainder of the careful physical examination were normal. Results of routine hematology panel were within normal ranges, with a total leukocyte count of 6.0×10^3/uL, hemoglobin 12.2 g/dL, derived hematocrit 34.8%, mean corpuscular volume 77.6 fl, mean corpuscular hemoglobin concentration 35.1/dL, mean corpuscular hemoglobin 37.1 pg, and quantitative platelet count 287,000. There were 1.2% reticulocytes. A review of peripheral blood smears showed mild hypochromasia and microcytosis and normal white cell morphology.

The following list shows the results of iron and copper studies:

Iron, serum	60 µg/dL
Total iron-binding capacity	374 µg/dL
Percent saturation	16
Unsaturated iron-binding capacity	314 µg/dL
Ferritin	20 ng/mL
Zn-protoporphyrin	24 µg/dL
Copper, serum	1,238 µg/L
Ceruloplasmin	26 mg/dL
Copper, urine	19.4 µg/g creatinine

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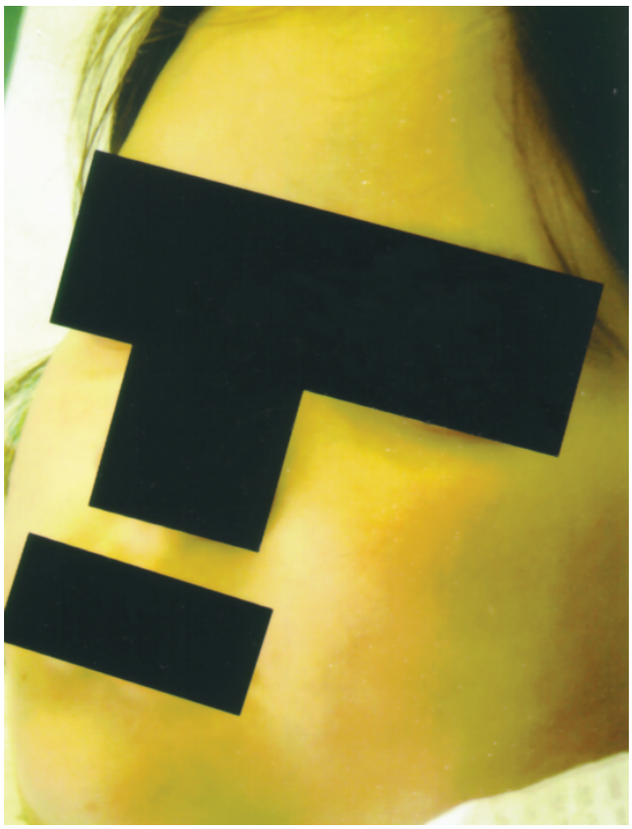

Figure 1. Nine-year-old girl with green skin tone and iron deficiency anemia.

Results of a comprehensive serum chemistry panel and liver panel results were within normal ranges. Results of factor VIII activity showed 88% activity, the von Willebrand factor antigen was at 143%, and the ristocetin cofactor was 121%.

Clinical Course

Because the results of the iron studies were conclusive for iron deficiency (MCV, ferritin, and iron saturation were in the low normal range) a trial of elemental iron, 4 mg/kg/day, was initiated. Within a few days the patient's green skin tone disappeared. She felt better and her energy and appetite had returned to normal.

Discussion

Medical chlorosis, the "green sickness," is characterized by a sallow-green facial complexion usually accompanied by iron-deficiency anemia in asthenic teenage girls and young unmarried women. A popular diagnosis in 18th, 19th, and early 20th centuries for young women with a number of psychological, gynecological, and/or gastrointestinal complaints, the diagnosis of chlorosis found its way into the common parlance of the day. Chlorosis rapidly diminished in the early 20th century as nutrition improved and hemoglobin determinations, easily performed by outpatient laboratories, enabled physicians to judiciously prescribe ferrous therapy at an early, preclinical stage of iron deficiency. By 1930, the abrupt disappearance of chlorosis led to speculation that the characteristic green complexion associated with the condition had been largely imagined by overzealous or copycat physicians, poets, and novelists. In 1987, Dr. William Crosby, a widely respected American hematologist, wrote a Commentary entitled: Whatever became of Chlorosis?[1]

Chlorosis is the name of either a common botanical disease of iron-deficient chlorophyll-containing plants or of a curious, supposedly extinct, disease of humans. A popular diagnosis in 18th, 19th, and early 20th centuries for young women with a number of psychological (anorexia nervosa, sexual frustration, or love-sickness), gynecologic (hysteria, excessive blood loss, or amenorrhea), and/or gastrointestinal (dyspepsia, peptic ulcer, vomiting, constipation) complaints, the diagnosis of chlorosis found its way into the common parlance of the day. In 1881, the *Index of Medical Literature*, the predecessor of the *Index Medicus*, contained more than 7 pages of references to human chlorosis.[1] In the 1890s, 2% of the admissions to the Allgemeine Krankenhaus in Vienna, Austria, and 16% of admissions to St. Bartholomew's Hospital in London, carried the diagnosis of chlorosis.[1] Monographs were written on chlorosis based on recollections at the time the diagnosis was in vogue.[2] The history of chlorosis has been well researched.[3-8] The diagnosis was also common in the novels and poetry of that era.[9] Starobinski[11] quotes the following English translation of a gravestone inscription composed on the tomb

of a French girl who was believed to have died of chlorosis; "Poor girl, how I pity you, Dying from a malady, For which there are so many physicians."[3] By 1910, only 3% of admissions at St. Bartholomew's had chlorosis, and in 1911, no cases were reported by the Krankenhaus in Vienna.[1] By 1930, the disease became virtually extinct in Europe and America. Nonetheless, this mysterious disease continues to maintain interest and be a source of fascination. Chlorosis, the "green sickness," appears on the internet and is the main subject of a nonfiction book published in 2003.[10]

Although various psychological (anorexia nervosa), neurologic, and gynecologic theories were promulgated to explain the pathophysiology of chlorosis, we now know that the major sign of the disease (green complexion) and major symptom (weakness) are caused by hypochromic microcytic red blood cells and total body iron deficiency. Starobinski,[11] Crosby,[1] and others deduced that there were several reasons for the demise of chlorosis, including the invention and widespread use of laboratory instruments to measure hemoglobin, the resultant prescriptions for therapeutic iron based on low hemoglobin percentages rather than clinical signs of pallor and weakness, and the overall improvement in nutrition in the working class. Curiously, the bizarre green facial complexion characteristic of chlorosis does not always appear, even when hemoglobin values are profoundly low. Crosby[1] speculates that the green color was caused by a codeficiency of iron and protein, but this theory and others remain highly speculative.[12-14]

In spite of her green complexion, our 9-year-old patient appeared otherwise well, with no evidence or history of liver disease, disorder of copper metabolism, hypoproteinemia, unhealthy diet, or eating disorder. A comprehensive laboratory evaluation revealed abnormal results only for iron deficiency with mild hypochromasia.

We believe that this is the first medically witnessed, well-documented, and photographed case of classical chlorosis in a young girl in the past 70 years. We offer no additional explanation for the characteristic green facial complexion of chlorosis but do confirm that it disappeared promptly after initiation of iron salt therapy.

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